Humphreys SC[1], Elbasha EH[2], Ferrante SA[2], Lion M[1], O'Regan C[1]
[1]Merck Sharp & Dohme Ltd., Hoddesdon, UK, [2]Merck Sharp & Dohme Corp., Whitehouse Station, NJ, USA

OBJECTIVES: Despite available treatment options, chronic infection of individuals with the hepatitis C virus (HCV), together with associated chronic liver diseases, remains a significant public health burden in England and Wales. Fewer than half of patients with genotype 1 chronic hepatitis C (CHC) achieve sustained virologic response (SVR) following the current standard treatment with peginterferon alfa and ribavirin. The aim of this analysis was to evaluate the cost-effectiveness of boceprevir, a protease inhibitor, in combination with peginterferon alfa and ribavirin, compared to peginterferon alfa and ribavirin alone, among treatment naïve and previously treated patients with genotype 1 CHC in England and Wales. **METHODS:** Specific treatment strategies for boceprevir have been outlined in the UK licence for different patient groups. A Markov model was developed to evaluate these treatment strategies for boceprevir triple-therapy compared to peginterferon alfa and ribavirin alone, and to estimate the expected costs and health-related quality of life benefits associated with them. The incremental cost-effectiveness of including boceprevir in a new triple-therapy standard of care was assessed from the perspective of the National Health Service and Personal Social Services over the lifetime of the patient cohort. Clinical data inputs for each treatment strategy were estimated based on subgroup analyses of the phase III trials for boceprevir. **RESULTS:** The incremental cost-effectiveness ratio (ICER) for treatment-naïve patients was £11,601 when boceprevir triple-therapy was compared to current standard treatment with peginterferon alfa and ribavirin. For treatment-experienced patients, the ICER with boceprevir triple-therapy was £2,909. These results were robust to sensitivity analyses and below a threshold of £20,000. **CONCLUSIONS:** The inclusion of boceprevir as part of a new triple-therapy standard of care for patients with genotype 1 CHC is clinically efficacious and cost-effective, irrespective of whether patients have been previously treated. The use of boceprevir in this setting is recommended by NICE.

PGI19

COSTS AND EFFECTS OF DUAL THERAPY WITH PEGYLATED INTERFERON AND RIBAVIRIN IN PATIENTS WITH CHRONIC HEPATITIS C IN GERMANY

Berg T[1], Buggisch P[2], Mauss S[3], Wedemeyer H[4], Benter U[5], Decker-Burgard S[6]
[1]Universitätsklinikum Leipzig, Leipzig, Germany, [2]Ifi-Institut Hamburg, Hamburg, Germany, [3]Center for HIV and Hepatogastroenterology, Duesseldorf, Germany, [4]Medizinische Hochschule Hannover, Hannover, Germany, [5]INC Research LLC, Munich, Germany, [6]Janssen-Cilag GmbH, Neuss, Germany

OBJECTIVES: Dual therapy with ribavirin and peg-interferon over a duration of up to 72 weeks (W) has been the former standard of care in patients with chronic Hepatitis C (HCV) genotype 1 and is still used in some patients. The aim of this analysis is to evaluate the direct HCV-related costs and effects of dual therapy in therapy-naïve and pretreated patients in Germany. **METHODS:** In this retrospective chart review study, dual therapy in patients with chronic HCV genotype 1 in 2008/2009 was evaluated in Germany. Data from patients treated with a combination of ribavirin and peg-interferon were retrospectively documented during the treatment period and thereafter (on average 61 W of post-treatment follow-up). A total of 208 therapy-naïve and 182 pretreated patients from 31 study sites were included in the analysis. **RESULTS:** Mean time since first diagnosis of HCV was 6.0 years and 10.4 years in therapy-naïve and pretreated patients, respectively. 33.0% of pretreated patients were prior non responders, 37.9% were relapsers. The average treatment duration during study was 42 W (SD 22W) both in therapy-naïve and pretreated patients. Sustained virological response (SVR) was demonstrated in 58.1% of therapy naïve and 36.6% of pretreated patients with HCV-RNA measurements available (167 and 142 patients with measurement, respectively). Mean per patient costs related to HCV during therapy from the statutory health insurance perspective were 14,554€ (SD 9,139€) for therapy-naïve and 14,590€ (SD 10,443€) for pretreated patients. Main cost-driver of treatment was medication cost, accounting for 87% of total costs, followed by sick leaves and diagnostics. Hospitalizations and physician visits played a less important role in terms of costs. **CONCLUSIONS:** Especially in pretreated patients, HCV dual therapy is costly due to the low treatment success rate. This emphasizes the need for treatments with improved efficacy, minimizing costly non-response resulting in potential cost savings.

PGI20

COST-EFFECTIVENESS OF ADALIMUMAB FOR TREATMENT OF CROHN'S DISEASE IN GERMANY

Yang M[1], Yang M[2], Skup M[2], Zhou ZY[1], Hengst N[3], Wolff M[3], Mulani PM[2], Chao J[2]
[1]Analysis Group, Inc., Boston, MA, USA, [2]Abbott Laboratories, Abbott Park, IL, USA, [3]Abbott GmbH & Co. KG, Ludwigshafen, Germany

OBJECTIVES: To assess cost-effectiveness of adalimumab versus standard care (SC) for treating patients with severely active Crohn's disease (CD) in Germany from a societal perspective. Additionally, cost-per-remitter for adalimumab was estimated and compared with infliximab 5mg/kg maintenance therapy. **METHODS:** To compare adalimumab to SC, a 4-disease-state clinical model (ie, remission, moderate, severe, very severe) based on the Crohn's Disease Activity Index (CDAI) was constructed tracking patients over their lifetimes. The model estimated direct costs, indirect costs, and quality-adjusted life-years (QALYs) from the German societal perspective. Efficacy inputs for adalimumab were based on actual observations from CHARM (Crohn's Trial of the Fully Human Antibody Adalimumab for Remission Maintenance). Using data from CLASSIC I (Clinical Assessment of Adalimumab Safety and Efficacy Studied as Induction Therapy in Crohn's Disease), a regression model was used to predict efficacy of SC. Direct/indirect costs and utility inputs were derived from public sources and literature. To compare adalimumab to infliximab, cost-per-remitter was estimated by dividing costs by the percentage of patients in remission on a yearly basis. Remission rates of adalimumab and infliximab upon baseline matching adjustment for patients with moderate-to-severe CD came from CHARM and ACCENT I (A Crohn's Disease Clinical Trial Evaluating Infliximab in a New Long-Term Treatment Regimen), respectively. **RESULTS:** The incremental costs per QALY gained for adalimumab versus SC were €37,270 (2012 Euro) over a lifetime horizon in the base case. One-way sensitivity analyses varying key parameters produced incremental costs per QALY gained ranging from €23,011–€51,528 when compared with SC. An average of 47.2% adalimumab-treated and 37.1% infliximab-treated patients were in remission yearly. The corresponding cost-per-remitter was €54,823 for adalimumab and €88,506 for infliximab. **CONCLUSIONS:** Adalimumab appears to be cost-effective compared with SC for treating patients with severely active CD. The cost-per-remitter for maintenance therapy was less for adalimumab than for infliximab.

PGI21

COST EFFECTIVENESS OF THE COMBINATION OF BOCEPREVIR PLUS PEGINTERFERON ALPHA AND RIBAVIRIN VERSUS TELAPREVIR PLUS PEGINTERFERON ALFA AND RIBAVIRIN IN THE RETREATMENT OF PATIENTS WITH CHRONIC HEPATITIS C VIRUS GENOTYPE I INFECTION

Fonseca M[1], Garran V[2], Araujo GT[3]
[1]Federal University of São Paulo/Axia.Bio Consulting, São Paulo, Brazil, [2]MSD, São Paulo, Brazil, [3]Axia.Bio Consulting, Sao Paulo, Sao Paulo, Brazil

OBJECTIVES: In patients with chronic infection with hepatitis C virus (HCV) genotype 1 who did not achieve a sustained response to the standard therapy with peginterferon/ribavirin (PR) the combination of boceprevir (B) or telaprevir (T) plus peginterferon alpha/ribavirin have shown to produce a higher rate of sustained virologic response (SVR) than the retreatment with PR. The aim of this study is to assess the cost effectiveness of these two (BPR and TPR) antiviral regimens. **METHODS:** We developed a Markov model to describe the clinical history of previously treated HCV genotype 1 patients who did not achieve SVR in which one cohort (1) receives PR for 4 weeks followed by BPR for 32 weeks and, those patients with a detectable HCV RNA level at week 8 receive PR for an additional 12 weeks; cohort 2 patients receive 12 weeks TPR followed by 36 weeks PR. All patients are followed for their expected lifetime. The reference patient is 30-year-old with CHC without cirrhosis. The SVRs to BPR and TPR cohorts came from RESPOND 2 and REALIZE studies. Quality of life for each health state was based on literature. Costs for each health state were based on three Delphi panels, one with hepatologists, one with intensivists and another with oncologists. Costs in 2011 Brazilian Reais and benefits were discounted at 3%. **RESULTS:** The combination BPR increases life expectancy by 0.60 years and quality adjusted life years (QALY) by 0.89 years compared to TPR. BPR is cheaper than TPR (-23,428 Brazilian Reais). **CONCLUSIONS:** In Brazil, for the treatment of previously treated patients with HCV genotype 1 infection boceprevir plus peginterferon alpha/ribavirin is dominant compared with telaprevir plus peginterferon alpha/ribavirin.

PGI22

COST-EFFECTIVENESS ANALYSIS OF DEXLANSOPRAZOLE FOR THE TREATMENT OF EROSIVE ESOPHAGITIS COMPARED TO CONVENTIONAL PROTON PUMP INHIBITORS

Valencia-Romero A[1], Gay-Molina JG[2], Chiu-Ugalde J[3], Figueroa-Rodriguez A[3], López-Alvarenga JC[4], Sánchez-Kobashi R[2], Vargas JA[3]
[1]Hospital de Alta Especialidad PEMEX Sur, Mexico City, Mexico, [2]Tecnología e Informática para la Salud, S.A. de C.V., Mexico City, Mexico, [3]Nycomed: A Takeda Company, Naucalpan, Edo. Mexico, Mexico, [4]Hospital General de México O.D., Mexico City, Mexico

OBJECTIVES: The study compares the cost-effectiveness (CE) of dexlansoprazole with other proton pump inhibitors (PPI) currently included in the Mexico National Formulary (Positive List) for treatment of erosive esophagitis (EE). **METHODS:** A decision tree with the 8-week temporal horizon was designed for patients over 18 with EE confirmed by endoscopy. The perspective taken is that of second-level public health institutions. Treatment alternatives modelled are dexlansoprazole 60 mg/day, esomeprazole 40 mg/day; omeprazole 20 mg/day, pantoprazole 40mg/day, rabeprazole 20 mg/day. Possible outcomes considered were healing or not healing, the latter possibly leading to surgery. Costs included in the model were treatment regimens, consult, endoscopy, surgery (when necessary), and hospitalization days (when necessary) and were taken from official or published sources. Effectiveness was measured in terms of percentage of patients with healed oesophagus. A weighted average of effectiveness was calculated for use in the model. One-way sensitivity analyses of cost and effectiveness variables and a Monte Carlo (MC) simulation of a 1000 cohorts were also conducted to test the robustness of the results. **RESULTS:** Compared to all PPIs modelled/tested, dexlansoprazole was highly dominant, being more effective (0.9270) and less costly (USD$ 1.27 per day), even when compared to omeprazole's USD$ 0.015 per DDD. It was therefore not considered necessary to calculate the Incremental Cost-Effectiveness Ratio (ICER) since these would be negative. The sensitivity analyses and Monte Carlosimulations found omeprazole to be the second-best alternative, and actually dominant in 16.7% of the MC simulations. **CONCLUSIONS:** Dexlansoprazole was found to be dominant compared to all PPIs evaluated for EE, being both more effective and less costly for public institutions in Mexico.

PGI23

COST-EFFECTIVENESS OF EPISODIC OR MAINTENANCE INFLIXIMAB VERSUS STANDARD TREATMENT IN AN INCIDENCE COHORT OF CROHN'S DISEASE PATIENTS WITH 10-YEARS FOLLOW-UP

Odes S[1], Greenberg D[2], Vardi H[2], Friger M[2], Stockbrugger R[3], Munkholm P[4]
[1]Soroka Medical Center, Beer-Sheva, Israel, [2]Ben Gurion University of the Negev, Beer-Sheva, Israel, [3]University Hospital Maastricht, Maastricht, The Netherlands, [4]Herlev Hospital and University of Copenhagen, Copenhagen, Denmark

OBJECTIVES: Infliximab is indicated in Crohn's disease (CD) resistant to standard treatment (ST), but its impact on health care costs and quality-adjusted life-expectancy is incompletely understood. We assessed the cost-effectiveness of episodic (ET) and maintenance (MT) infliximab treatment in CD patients with 10-years follow-up. **METHODS:** A total of 212 incident adult CD patients (age at onset 34.4±14.5 years, 49.4% male) were treated with antibiotics, mesalazine, corticosteroids, thiopurines, surgery (comprising ST) over 10-years to 2004. Eight health states were defined by intensity of therapy in these patients. We determined Markov transition probabilities between these states, health care costs and QALYs in 3 month-cycles. This cohort was modeled to allow drug-refractory or pre-surgery patients to receive infliximab: either ET in one cycle, or MT in responders for a period of 1-year (MT-1yr) or for 10-years (MT-10 yrs). Transition probabilities of ST were applied to patients getting IFX; the probability of continuing infliximab in MT was set to correct for decay. Health care costs and QALYs in ET and MT were estimated for 10-years (discounted at 3%) and compared with those of ST patients. **RESULTS:** The average cost (QALYs gained) per patient over 10-years was €23,169 (6.7014) for ST; €21,691 (7.0403) for ET, €29,012 (7.0553) for MT-1yr, and €50,416 (7.2603) for MT-10 yrs. ST was associated with higher costs and lower outcomes and was thus dominated by ET. The incremental cost-effectiveness ratios (ICERs) of MT-1yr and MT-10 yrs over ST were €16,510/QALY gained, and €48,751/QALY gained, respectively. When compared with ET, the ICERs of MT-1yr and MT-10 yrs were €488,066/QALY gained, and €130,568/QALY gained, respectively. When the infliximab price was halved these ICERs remained very high. **CONCLUSIONS:** ET or MT with infliximab are either cost-saving or cost-effective when compared with ST. However, at current drug prices, MT does not provide good value for money when compared with ET.

PGI24

COST-EFFECTIVENESS ANALYSIS OF 48-WEEK PEGINTERFERON ALPHA-2A UNDER RGT STRATEGY VERSUS 3 YEARS ENTECAVIR FOR THE TREATMENT OF HBEAG-POSITIVE CHRONIC HEPATITIS B IN CHINA

Zhang W[1], Zhuang H[2], Ren H[3], Dou X[4], Chen W[5]
[1]Huashan Hospital Medical Center of Fudan University, Shanghai, China, [2]Peking University Health Science Center, Beijing, China, [3]Second Affiliated Hospital of Chongqing University of Medical Science, Chongqing, China, [4]Shengjing Hospital of China Medical University, Shenyang, China, [5]Fudan University, Shanghai, China

OBJECTIVES: To evaluate direct medical costs, health outcomes, and cost-effectiveness of 48-week Peginterferon alpha-2a with 2nd line 2-years Entecavir treatment versus 3 years Entecavir treatment for HBeAg-positive chronic hepatitis B according to the Response Guided Treatment (RGT) strategy in China. **METHODS:** A Markov model was designed to evaluate the direct medical costs and outcomes (life years and QALYs gained) of treating HBeAg-positive chronic hepatitis B in China, with a maximum analysis time horizon of 80 years. The model included 10 health states – Chronic hepatitis B (CHB), HBeAg seroconversion, HBsAg loss, CHB with resistance, Compensated cirrhosis, Decompensated cirrhosis, Hepatocellular carcinoma, Liver transplant, Post-liver transplant and death. Based on the analysis of published literature, a two-round expert panel survey was conducted among 22 hepatitis B specialists nationally to identify clinical and utility data. From the perspective of China's health insurance system, cost data was calculated based on the published literature about CHB economic burden. A discounting rate at 3% was used to discount medical costs and health outcomes that happened at different years. A univariate sensitivity analysis was performed to understand the key drivers and general sensitivity of the model. **RESULTS:** The model results showed that the utilization of Peginterferon regimen can prolong1.80 QALYs (15.00 years vs. 13.20 years), compared to the 3 years Entecavir treatment. The total cost per patient treated with Peginterferon and Entecavir was RMB 163,638 yuan (US$ 25,568) and RMB 145,116 yuan (US$ 22,674), respectively. The discounted incremental cost per QALY gained for Peginterferon regimen was RMB 10,298 yuan (US$ 1,609) (Exchange rate: 1 US$ = 6.4 CNY). **CONCLUSIONS:** The results of the model suggest that 48-week Peginterferon alpha-2a with 2-years Entecavir treatment as 2nd line improves health outcomes in a cost-effective manner compared with 3 years Entecavir for the treatment of HBeAg-positive chronic hepatitis B in China.

PGI25

COST-UTILITY ANALYSIS OF TELAPREVIR IN COMBINATION WITH PEGINTERFERON ALPHA AND RIBAVIRIN IN PREVIOUSLY TREATED PATIENTS WITH CHRONIC HEPATITIS C

Lukac M[1], Bielik J[2], Holoman J[3], Tomek D[4], Suvadova A[5], Foltanova T[6], Foltan V[7]
[1]Slovak Medical University, Bratislava, Slovak Republic, [2]Trencin University, Trencin, Slovak Republic, [3]National Reference Center for Managment and Therapy of Chronic Hepatitis, Bratislava, Slovak Republic, [4]Pharmaceutical Faculty at Comenius University, Bratislava, Slovak Republic, [5]Janssen, Bratislava, Slovak Republic, [6]Faculty of Pharmacy, Bratislava, Slovak Republic, [7]Faculty of Pharmacy, Comenius University, Bratislava, Slovak Republic

OBJECTIVES: To estimate the cost-effectiveness of telaprevir in combination with peginterferon alpha and ribavirin (PR) compared to PR alone in previously treated patients. **METHODS:** A cost-utility analysis based on previously published Markov models for chronic hepatitis C was used. Efficacy in the model was derived from results of randomized placebo controlled trial (REALIZE). REALIZE compared telaprevir in combination with PR to PR alone in patients who failed previous treatment. The trial showed significantly higher response rates in the telaprevir patient cohort. Utility values corresponding to each health state in the model were obtained from a NICE Health technology Assessment and were combined with data from REALIZE. Local cost data sources were from published price lists, clinical guidelines, product labels and expert opinion (DELPHI panel). The effectiveness was measured in quality-adjusted life years (QALY). Time horizon was set at lifelong (100 years of age or till patient dies) and a payers' perspective was adopted. Discount rate was 5% per year for both costs and effects according to actual Ministry of Health guidelines for health economic evaluation. Both one-way and probabilistic sensitivity analyses were performed. **RESULTS:** Incremental cost effectiveness ratio (ICER) for telaprevir in combination with PR compared to PR alone was 14 209 €/1 QALY. Costs for one life year saved (LYS) were 20 026 €/1 LYS. Model was most sensitive to price of telaprevir in deterministic sensitivity analysis. In probabilistic sensitivity analysis 75 % of simulations were below 26 650 €/1 QALY. **CONCLUSIONS:** Telaprevir in combination with PR is a cost-effective compared to PR alone for the treatment of chronic hepatitis C in patient who failed previous treatment with PR in a Slovakian health care system.

PGI26

WITHIN-TRIAL ANALYSIS TO ESTIMATE THE ECONOMICALLY JUSTIFIABLE PRICE OF LINACLOTIDE IN THE TREATMENT OF IRRITABLE BOWEL SYNDROME WITH CONSTIPATION IN THE UK

McDonell A[1], Barzey V[1], Kotchie R[1], Mungapen L[1], Prior M[2], Fortea J[2]
[1]IMS, London, UK, [2]Almirall, Barcelona, Spain

OBJECTIVES: Linaclotide is a novel once daily, orally delivered peptide that acts on all key IBS-C symptoms. The aim of this analysis was to estimate the daily cost that would result in linaclotide being considered cost-effective in the UK, given different levels of willingness–to-pay (WTP). **METHODS:** A within-trial analysis was used to estimate the economically justifiable price from a payer perspective in the UK using patient-level data from a 26-week Phase III, randomized, double-blind trial of linaclotide 290μg daily (n=401) versus placebo (n=403) in IBS-C patients (modified Rome II criteria). EQ-5D data was collected at randomization and each subsequent visit. The UK valuation of the EQ-5D was applied to the raw data to estimate the utility for each patient. Missing data were interpolated using the last-observation-carried-forward (LOCF) method. The WTP was varied from £15,000-£20,000/QALY. The only cost considered was that of linaclotide; total cost of treatment was weighted by compliance. Resource use was assumed to be equal between arms. Bootstrapping was performed to account for uncertainty. A scenario analysis was conducted using data from a 12-week linaclotide trial in a similar population. **RESULTS:** Patients treated with linaclotide gained 0.016 QALYs over the 26-week trial compared with patients in the placebo arm. At WTP thresholds of £15,000-£20,000/QALY linaclotide could be cost-effective at a price of £1.30-£1.70. Over 75% of the bootstrap estimates fell below a willingness-to-pay threshold of £20,000/QALY. The method of addressing missing data had minimal impact on the ICER. In the scenario analysis, the QALY gain for patients treated with linaclotide was even greater, thus a price of £2.00-£2.65 may result in linaclotide being considered cost-effective at thresholds of £15,000-£20,000/QALY. **CONCLUSIONS:** The base case analysis showed linaclotide could be cost-effective at a price of up to £1.70/day in the UK setting using conservative assumptions.

PGI27

IMPACT OF LINACLOTIDE TREATMENT ON WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN ADULTS WITH IRRITABLE BOWEL SYNDROME WITH CONSTIPATION

Buono JL[1], Tourkodimitris S[1], Sarocco P[2], Baird MJ[2], Johnston JM[2], Carson R[1]
[1]Forest Research Institute, Jersey City, NJ, USA, [2]Ironwood Pharmaceuticals, Cambridge, MA, USA

OBJECTIVES: Irritable bowel syndrome with constipation (IBS-C) can decrease work productivity and increase activity impairment, resulting in a substantial economic burden for patients and employers. Linaclotide, a minimally-absorbed guanylate cyclase C agonist (GCCA), significantly improved abdominal and bowel symptoms in 2 Phase 3 IBS-C trials. We evaluated the linaclotide treatment effect on work productivity and activity impairment in IBS-C patients. **METHODS:** In 2 Phase 3 trials, 1602 adults with IBS-C (modified Rome II criteria) were randomized to oral linaclotide 290 μg once daily or placebo. The self-administered 6-item Work Productivity and Activity Impairment questionnaire for IBS-C (WPAI:IBS-C) was used to evaluate IBS-C symptom-related absenteeism (work hours missed), presenteeism (degree symptoms affected work productivity), overall work productivity loss (absenteeism+presenteeism) and daily activity impairment (degree symptoms affected activities) over the previous week. Using pooled intent-to-treat data, changes in WPAI:IBS-C scores from baseline to Weeks 4, 8, and 12 were assessed by analysis of covariance and represented as percentages (higher percentage=greater productivity loss and activity impairment). Absenteeism, presenteeism and work productivity assessments included employed patients only. **RESULTS:** Compared to placebo, linaclotide significantly reduced presenteeism, overall work productivity loss and daily activity impairment, and numerically decreased absenteeism, at Weeks 4, 8 and 12. Mean changes from baseline to Week-12 for linaclotide and placebo, and the corresponding treatment effect (LS-means difference between linaclotide and placebo, shown as "Δ"), respectively, were: presenteeism, -18.4% and -13.1% (Δ=-5.2, P<0.0001); overall work productivity loss, -19.4% and -13.0% (Δ=-6.1, P<0.0001); daily activity impairment, -19.9% and -15.2%(Δ=-4.7, P<0.0001); absenteeism, -1.6% and -0.9% (Δ=-0.5, P=0.311). Assuming a 40-hour work week, linaclotide reduced overall work productivity loss by 1.6-2.4 hours/week. **CONCLUSIONS:** Linaclotide significantly reduced presenteeism, overall work productivity loss and daily activity impairment for IBS-C patients